

Appl. No. 09/899,552
Response dated April 22, 2005
Reply to Office action of March 22, 2005

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Original) A method of ranking the immune response of a test animal within a population of animals under stress comprising:
 - (a) immunizing the animals with at least one antigen at least once before the onset of the stress; and
 - (b) measuring the antibody response of the animals to the at least one antigen at least once before the onset of the stress and at least once during the stress,
wherein a change in antibody response from before the onset of stress to during the stress for the test animal that is greater than the average change in antibody response from before the onset of the stress to during the stress for the population indicates that the animal is a high immune responder.
2. (Original) A method of ranking the immune response of a test animal within a population of animals under stress comprising:
 - (a) immunizing the animals with at least one antigen at least once before the onset of the stress and at least once during the stress; and
 - (b) measuring the antibody response of the animals to the at least one antigen at least once before the onset of the stress and at least once during the stress,
wherein a change in antibody response from before the onset of stress to during the stress for the test animal that is greater than the average change in antibody response from before the onset of the stress to during the stress for the population indicates that the animal is a high immune responder.
3. (Original) A method of ranking the immune response of a test animal within a population of animals under stress comprising:

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(a) immunizing the animals with at least one antigen at least once before the onset of the stress and at least once during the stress; and

(b) measuring the antibody response of the animals to the at least one antigen at least once before the onset of the stress and at least twice during the stress, wherein the changes in antibody responses between each measurement are added to provide a total antibody response and a total antibody response for the test animal that is greater than an average total antibody response for the population indicates that the animal is a high immune responder.

4. (Original) The method according to claim 3, wherein negative changes in antibody responses during the stress are multiplied with a co-efficient greater than 1.
5. (Original) The method according to claim 4, wherein negative changes in antibody responses during the stress are multiplied with a co-efficient of about 1.5.
6. (Original) The method according to claim 3, wherein the stress is selected from the group consisting of disease, weaning, castration, dehorning, branding, shipping, change in ration, social disruption, restraint, periparturition and exercise.
7. (Original) The method according to claim 6, wherein the stress is periparturition.
8. (Original) The method according to claim 1, wherein the animal is bovine.
9. (Original) The method according to claim 8, wherein the bovine is selected from a multiparous cow and a primiparous cow.
10. (Original) The method according to claim 8, wherein the bovine is a multiparous cow.

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11. (Original) The method according to claim 1, wherein the antigen is selected from the group consisting of hen egg white lysozyme, human serum albumin, tyrosine-glycine-alanine-lysine copolymer and ovalbumin.
12. (Original) The method according to claim 11, wherein the antigen is ovalbumin.
13. (Original) The method according to claim 12, wherein the antigen is formulated with an adjuvant selected from the group consisting of Freund's complete adjuvant (FCA), non-ulcerative Freund's adjuvant (NUFA), complete NUFA and *mycobacteria* cell wall extract.
14. (Original) The method according to claim 1, wherein the antigen is formulated into a vaccine.
15. (Original) The method according to claim 14, wherein the vaccine is *Escherichia coli* J5.
16. (Original) The method according to claim 1, wherein a source for measuring the antibody response is selected from the group consisting of blood and milk.
17. (Original) The method according to claim 7, wherein the measuring of the antibody response at least once before the onset of the stress is at about 8 weeks before parturition and the measuring of the antibody response at least once during the stress is at about 3 weeks before parturition and at about parturition.
18. (Original) The method according to claim 7, wherein the measuring of the antibody response at least once before the onset of the stress is at about 8 weeks before parturition and the measuring of the antibody response at least once during the stress is at about 3 weeks before parturition, at about parturition and at about 3 weeks after parturition.

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19. (Original) The method according to claim 7, wherein the immunizing the animals at least once before the onset of the stress is at about 8 weeks before parturition and the immunizing the animals at least once during the stress is at about 3 weeks before parturition and at about parturition.

20. (Original) The method according to claim 7, wherein the immunizing the animals at least once before the onset of the stress is at about 8 weeks before parturition and the immunizing the animals at least once during the stress is at about 3 weeks before parturition, at about parturition and at about 3 weeks after parturition.

21. (Original) A method of ranking the immune response of a test animal within a population of animals under stress comprising:

(a) immunizing the animals with at least one antigen at least once before the onset of the stress;

(b) measuring the antibody response of the animals to the at least one antigen at least once before the onset of the stress and at least once during the stress; and

(c) calculating a mathematical index of the antibody response, wherein the mathematical index is: y = primary antibody response, wherein

(i) y is the immune response; and

(ii) the primary response is the difference in antibody quantity at a first time point before the onset of stress and a second time point during the stress, wherein the animal is immunized at the first time point before the onset of stress;

wherein a test animal having a y value greater than about one standard deviation above the average of the y value for the population is a high immune responder.

22. (Original) A method of ranking the immune response of a test animal within a population of animals under stress comprising:

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(a) immunizing the animals with at least one antigen at least once before the onset of the stress and at least once during the stress;

(b) measuring the antibody response of the animals to the at least one antigen at least once before the onset of the stress and at least two times during the stress; and

(c) calculating a mathematical index of the antibody response, wherein the mathematical index is: $y = \text{primary antibody response} + \text{secondary antibody response}$, wherein

(i) y is the immune response;

(ii) the primary response is the difference in antibody quantity at a first time point before the onset of stress and a second time point during the stress, wherein the animal is immunized at the first time point before the onset of stress; and

(iii) the secondary response is the difference in antibody quantity at a second time point during the stress and at a third time point during the stress, wherein the animal is immunized at the second time point during the stress;

wherein with animals exhibiting a negative secondary response, the secondary response is weighted with a co-efficient greater than 1, and a test animal having a y value greater than about one standard deviation above the average of the y value for the population is a high immune responder.

23. (Original) A method of ranking the immune response of a test animal within a population of animals under stress comprising:

(a) immunizing the animals with at least one antigen at least once before the onset of the stress and at least twice during the stress;

(b) measuring the antibody response of the animals to the at least one antigen at least once before the onset of the stress and at least three times during the stress; and

(c) calculating a mathematical index of the antibody response, wherein the mathematical index is: $y = \text{primary antibody response} + \text{secondary antibody response} + \text{tertiary antibody response}$, wherein

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- (i) y is the immune response;
- (ii) the primary response is the difference in antibody quantity at a first time point before the onset of stress and a second time point during the stress, wherein the animal is immunized at the first time point before the onset of stress;
- (iii) the secondary response is the difference in antibody quantity at a second time point during the stress and at a third time point during the stress, wherein the animal is immunized at the second time point during the stress; and
- (iv) the tertiary response is the difference in antibody quantity at a third time point during the stress and at a fourth time point during the stress, wherein the animal is immunized at the third time point during the stress;

wherein with animals exhibiting negative secondary and/or tertiary antibody responses, the secondary and/or tertiary antibody responses are weighted with a co-efficient greater than 1, and a test animal having a y value greater than about one standard deviation above the average of the y value for the population is a high immune responder.

24. (Original) A method of ranking the immune response of a test animal within a population of animals under stress comprising:

- (a) immunizing the animals with at least one antigen at least once before the onset of the stress and at least twice during the stress;
- (b) measuring the antibody response of the animals to the at least one antigen at least once before the onset of the stress and at least four times during the stress; and
- (c) calculating a mathematical index of the antibody response, wherein the mathematical index is: $y = \text{primary antibody response} + \text{secondary antibody response} + \text{tertiary antibody response} + \text{quaternary antibody response}$, wherein

- (i) y is the immune response;

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(ii) the primary response is the difference in antibody quantity at a first time point before the onset of stress and a second time point during the stress, wherein the animal is immunized at the first time point before the onset of stress;

(iii) the secondary response is the difference in antibody quantity at a second time point during the stress and at a third time point during the stress, wherein the animal is immunized at the second time point during the stress;

(iv) the tertiary response is the difference in antibody quantity at a third time point during the stress and at a fourth time point during the stress, wherein the animal is immunized at the third time point during the stress; and

(v) the quaternary response is the difference in antibody quantity at a fourth time point during the stress and at a fifth time point after the stress;

wherein with animals exhibiting negative secondary and/or tertiary antibody responses the secondary and/or tertiary antibody responses are weighted with a co-efficient greater than 1, and a test animal having a y value greater than about one standard deviation above the average of the y value for the population is a high immune responder.

25. (Withdrawn) A method of ranking the immune response of a test animal within a population of animals under stress comprising:

- (a) immunizing the animals with at least one antigen at least once before the onset of the stress;
- (b) measuring the antibody response of the animals to the at least one antigen at least once before the onset of the stress and at least once during the stress;
- (c) exposing the animals to an antigen which can evoke a cell-mediated immune response (CMIR); and
- (d) measuring at least one indicator of the CMIR in the animals during the stress,

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wherein the changes in antibody responses between each measurement are added to provide a total antibody response and the measurement of the indicator is combined with the total antibody response to provide an immune response and a test animal having an immune response that is greater than an average immune response for the population indicates that the animal is a high immune responder.

26. (Withdrawn) The method according to claim 25, wherein in (a) the animals are immunized with at least one antigen before the onset of stress and at least once during stress.

27. (Withdrawn) The method according to claim 25, wherein the indicator is selected from the group consisting of cytokines, delayed-type hypersensitivity and *In vitro* lymphocyte proliferation to at least one antigen.

28. (Withdrawn) The method according to claim 27, wherein the indicator is delayed-type hypersensitivity.

29. (Withdrawn) The method according to claim 28, wherein the antigen which can invoke a CMIR is selected from the group consisting of an intracellular organism and a mitogen.

30. (Withdrawn) The method according to claim 29, wherein the Intracellular organism is selected from the group consisting of *Mycobacterium bovis* and *Mycobacterium phlei*.

31. (Withdrawn) The method according to claim 29, wherein the mitogen is selected from the group consisting of concanavalin A and phytohaemagglutinin.

32. (Withdrawn) The method according to claim 29, wherein the antigen further comprises an adjuvant selected from the group consisting of Freund's complete adjuvant

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(FCA), non-ulcerative Freund's adjuvant (NUFA), complete NUFA and *mycobacteria* cell wall extract.

33. (Withdrawn) A method of ranking the immune response of a test animal within a population of animals under stress comprising:

(a) immunizing the animals with at least one antigen at least once before the onset of the stress;

(b) measuring the antibody response of the animals to the at least one antigen at least once before the onset of the stress and at least once during the stress;

(c) exposing the animals to an antigen which can evoke a cell-mediated immune response (CMIR);

(d) measuring at least one indicator of the CMIR in the animals during the stress; and

(e) calculating a mathematical index of the antibody response and CMIR, wherein the mathematical index is: $y = \text{primary antibody response} + \text{CMIR}$, wherein

(i) y is the immune response;

(ii) the primary response is the difference in antibody quantity at a first time point before the onset of stress and a second time point during the stress, wherein the animal is immunized at the first time point before the onset of stress;

(iii) CMIR is the measurement obtained from at least one method of determining CMIR,

wherein a test animal having a y value greater than about one standard deviation above the average of the y value for the population is a high immune responder.

34. (Withdrawn) A method of ranking the immune response of a test animal within a population of animals under stress comprising:

(a) immunizing the animals with at least one antigen at least once before the onset of the stress and at least once during the stress;

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(b) measuring the antibody response of the animals to the at least one antigen at least once before the onset of the stress and at least two times during the stress;

(c) exposing the animals to an antigen which can evoke a cell-mediated immune response (CMIR);

(d) measuring at least one indicator of the CMIR in the animals during the stress; and

(e) calculating a mathematical index of the antibody response and CMIR, wherein the mathematical index is: $y = \text{primary antibody response} + \text{secondary antibody response} + \text{CMIR}$, wherein

(i) y is the immune response;

(ii) the primary response is the difference in antibody quantity at a first time point before the onset of stress and a second time point during the stress, wherein the animal is immunized at the first time point before the onset of stress;

(iii) the secondary response is the difference in antibody quantity at a second time point during the stress and at a third time point during the stress, wherein the animal is immunized at the second time point during the stress; and

(iv) CMIR is the measurement obtained from at least one method of determining CMIR,

wherein with animals exhibiting a negative secondary response, the secondary response is weighted with a co-efficient greater than 1, and a test animal having a y value greater than about one standard deviation above the average of the y value for the population is a high immune responder.

35. (Withdrawn) A method of ranking the immune response of a test animal within a population of animals under stress comprising:

(a) immunizing the animals with at least one antigen at least once before the onset of the stress and at least twice during the stress;

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(b) measuring the antibody response of the animals to the at least one antigen at least once before the onset of the stress and at least three times during the stress;

(c) exposing the animals to an antigen which can evoke a cell-mediated immune response (CMIR);

(d) measuring at least one indicator of the CMIR in the animals during the stress; and

(e) calculating a mathematical index of the antibody response and CMIR, wherein the mathematical index is: $y = \text{primary antibody response} + \text{secondary antibody response} + \text{tertiary antibody response} + \text{CMIR}$, wherein

(i) y is the immune response;

(ii) the primary response is the difference in antibody quantity at a first time point before the onset of stress and a second time point during the stress, wherein the animal is immunized at the first time point before the onset of stress;

(iii) the secondary response is the difference in antibody quantity at a second time point during the stress and at a third time point during the stress, wherein the animal is immunized at the second time point during the stress;

(iv) the tertiary response is the difference in antibody quantity at a third time point during the stress and at a fourth time point during the stress, wherein the animal is immunized at the third time point during the stress; and

(v) CMIR is the measurement obtained from at least one method of determining CMIR.

wherein with animals exhibiting negative secondary and/or tertiary antibody responses, the secondary and/or tertiary antibody responses are weighted with a co-efficient greater than 1, and a test animal having a y value greater than about one standard deviation above the average of the y value for the population is a high immune responder.

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36. (Withdrawn) A method of ranking the immune response of a test animal within a population of animals under stress comprising:

(a) immunizing the animals with at least one antigen at least once before the onset of the stress and at least twice during the stress;

(b) measuring the antibody response of the animals to the at least one antigen at least once before the onset of the stress and at least four times during the stress;

(c) exposing the animals to an antigen which can evoke a cell-mediated immune response (CMIR);

(d) measuring at least one indicator of the CMIR in the animals during the stress;
and

(e) calculating a mathematical index of the antibody response and CMIR, wherein the mathematical index is: $y = \text{primary antibody response} + \text{secondary antibody response} + \text{tertiary antibody response} + \text{quaternary antibody response} + \text{CMIR}$, wherein

(i) y is the immune response;

(ii) the primary response is the difference in antibody quantity at a first time point before the onset of stress and a second time point during the stress, wherein the animal is immunized at the first time point before the onset of stress;

(iii) the secondary response is the difference in antibody quantity at a second time point during the stress and at a third time point during the stress, wherein the animal is immunized at the second time point during the stress;

(iv) the tertiary response is the difference in antibody quantity at a third time point during the stress and at a fourth time point during the stress, wherein the animal is immunized at the third time point during the stress;

(v) the quaternary response is the difference in antibody quantity at a fourth time point during the stress and at a fifth time point after the stress;
and

(vi) CMIR is the measurement obtained from at least one method of determining CMIR,

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wherein with animals exhibiting negative secondary and/or tertiary antibody responses, the secondary and/or tertiary antibody responses are weighted with a co-efficient greater than 1, and a test animal having a y value greater than about one standard deviation above the average of the y value for the population is a high immune responder.

37. (Withdrawn) The method according to claim 25, wherein the stress is parturition.

38. (Withdrawn) The method according to claim 36, wherein the stress is parturition and the first time point before the onset of stress is at about 8 weeks before parturition, the second time point during the stress is at about 3 weeks before parturition, the third time point during stress is parturition, and the fourth time point during stress is at about 3 weeks after parturition.